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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,142	10/30/2003	Charles P. Semba	P1989R1	9767

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EXAMINER	
UNDERDAHL, THANE E	
ART UNIT	**PAPER NUMBER**
1651	

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08/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/697,142	SEMBA, CHARLES P.	
	Examiner	Art Unit	
	Thane Underdahl	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the Applicant's reply received 6/04/07. Claims 1-7 are pending. No claims are withdrawn. Claims 8-35 are cancelled. Claim 7 has been amended.

Response to Applicant's Arguments— 35 U.S.C § 103

In the response submitted by the Applicant, the 35 U.S.C § 103 rejection of claims 1-7 over Sandbaek et al. in view of Graney with support from DrugBank were considered but not found persuasive.

Primarily the Applicant argues that Tenecteplase and Alteplase are not, as suggested by DrugBank, synonyms. While Applicant submits art from Kline et al. that successfully proves this point, the rejection as applied remains. Kline et al. indicates that Tenecteplase has a longer half-life than Alteplase (Kline, page 101, col 2, paragraph 1). While these enzymes are not identical they are, as taught by Kline et al., closely related as a parent enzyme (Alteplase) and its mutant (Tenecteplase) (Kline see Abstract and page 101, col 1, Introduction). These enzymes both perform the same reaction, namely their in-vivo fibrinolytic activity (Kline, page 101, col 2, paragraph 1) and both are used to break up thrombi (Sandbaek, see abstract, Kline page 102 patient data presented by Melzer et al. [18]). Given that each enzyme has close structural similarity and catalytic activity towards the dissolution of thrombi, the M.P.E.P. § 2144.09 states:

> "A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities"

Absent any evidence of criticality to the contrary one of ordinary skill in the art would expect the similar results for the Alteplase as that for Tenecteplase claimed by Applicant.

Furthermore since these enzymes have the same catalytic reaction, they are therefore art recognized equivalents for the same purpose and it would be obvious for one of ordinary skill in the art to substitute Tenecteplase for Alteplase (M.P.E.P. § 2144.06) and absent any evidence of criticality to the effect of their concentrations in solution on the reaction, it remains obvious to use the same concentration of Tenecteplase as you would for Alteplase.

The Applicant further argues the current invention is "useful for treating pathological collection of fibrin-rich fluid in the catheter, to provide catheter cleansing" (Applicant's response, page 3 last paragraph). However this is not commensurate to the scope of the claims which are to a composition and not a method. As a composition, the invention is defined by its components and the limitations implied in the intended use are considered only if they impart a structural limitation (see M.P.E.P. § 2111.02 II).

The Applicant argues that the solution of Sandbaek et al. is not allowed to dwell in the catheter. However this is not persuasive to the Examiner since the Applicant did not define the term "dwell" in the specification. Therefore the broad use interpretation of the common definition as provided by Merriam-Webster Online where dwell means "to remain for a time". It is clear that the indwelling catheter (Sandbaek page 88, col 1, paragraph 1) has a less than instantaneous rate of administration where the 25 mL of

the 0.2 mg/mL of Alteplase is added over the course of an hour. Therefore the Alteplase solution indeed remains for a time in the catheter and as such "dwells" in the catheter.

The Applicant argues that Graney does not cover the deficiency of Sandbaek by not mentioning the use of Tenecteplase and that Graney and Sandbaek teach the use of Alteplase for a treatment of thrombi and not for clearing out a catheter. However as mentioned previously, these claims are to a composition and not a method. As a composition, the invention is defined by its components and the limitations implied in the intended use are considered only if they impart a structural limitation (see M.P.E.P. § 2111.02 II).

Therefore the rejections stands and is repeated below with alternations to address the amended claim 7.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sandbaek et al. (Blood Coagulation and Fibrinolysis, 1999) as supported by DrugBank (def "Tenecteplase") in view of Graney et al. (Australian Patent AU-B-42810, published 1992).

These claims are drawn to a composition containing about 0.01 to 0.05 mg/mL of Tenecteplase in sterile water or bacteriostatic water and normal saline. Claims 2-5 further limit the range of the highest concentration of Tenecteplase in solution to about 0.04 mg/mL, 0.03 mg/mL, 0.02 mg/mL, 0.015 respectively. Claim 6 further limits the Tenecteplase be in sterile water. Claim 7 limits the composition of claim 1 further comprises an indwelling catheter. While Sandbaek does not expressly teach that the catheter is not occluded, it would have been obvious to someone skilled in the art not to use an occluded or blocked catheter since this would effect the flow of the Alteplase solution to the thrombi and as such be counterproductive to the teachings of Sandbaek that desires Alteplase solution access to dissolve the thrombi.

Sandbaek et al. teach a concentration of Alteplase in saline at a final concentration of 0.02 mg/mL and is administered by an indwelling catheter (page 88, col 1, "Intra-arterial thrombolysis"). Alteplase is an art recognized equivalent for the same purpose as Tenecteplase (M.P.E.P. § 2144.06). Sandbaek et al. does not teach the limitation of claim 5 that the concentration of Tenecteplase is about 0.01 to 0.015. However, the M.P.E.P. § 2145.05 state:

"a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties."

Also while the Sandbaek et al. above teaches the components of the composition of claim 1 they do not teach the concentration limited by claim 5. However, M.P.E.P. § 2144.05 II states:

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical.

Absent any teaching of criticality by the applicant concerning the concentration of Tenecteplase listed in claim 5 for the composition of claim 1, it would be *prima facie* obvious that one of ordinary skill in the art would recognize that the amounts listed in claim 5 are result effective variables whose ratio and concentration are a matter of routine optimization.

Also while Sandbaek et al. teach their composition in saline, they do not provide the details on the composition of the saline and thus do not anticipate the limitation of sterile water for injection or bacteriostatic water for injection and normal saline. This is taught by Graney et al.

Graney et al. teach that Tenecteplase (called the synonym tPA or tissue plasminogen activator or Alteplase by Graney, page 7, lines 1-2) can be included in compositions where the solvent carrier is sterile water (page 7, line 8) or distilled water, Ringer's solution as well as saline and other conventional carriers (page 8, lines 19 and 20). Therefore Graney et al. teach that saline as well as sterile water for injection and other conventional pharmaceutical carriers can be used interchangeably to dissolve and administer Tenecteplase and are therefore art recognized equivalents for the same purpose and it would be obvious for one of ordinary skill in the art to substitute saline from sterile water for injection (M.P.E.P. § 2144.06).

Therefore, the invention as a whole would have been prima facie obvious at the time of filing in view of the references listed above and as such claims 1-7 are not allowable.

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 7 includes the phrase "An indwelling catheter with no occlusions wherein". It is unclear if the occlusions are actually in the catheter or outside attached to the catheter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 7 includes the phrase "An indwelling catheter with no occlusions wherein". There is no description the Examiner could find in the Applicant's

specification that defines a "catheter with no occlusions". To overcome this rejection please simply site page and line for the support for this amendment in the specification.

In summary no claims, as written, are allowed for this application.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached Monday through Thursday, 8:00 to 17:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Thane Underdahl

Leon B. Lankford Jr

BLAINE LANKFORD
PRIMARY EXAMINER